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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/600,751

06/20/2003

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

05/07/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/600,751

Applicant(s)

BLEDSON ET AL.

Examiner

David J. Steadman

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-45 and 113-122 is/are pending in the application.
- 4a) Of the above claim(s) 113 and 121 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-45, 114-120 and 122 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Status of the Application

- [1]** Claims 38-45 and 113-122 are pending in the application.
- [2]** Applicant's amendment to claims, filed on 10/18/06, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3]** Applicant's amendment to the specification, filed on 10/18/06, is acknowledged.
- [4]** Applicant's arguments filed on 10/18/06 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [5]** The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

- [6]** Claims 113 and 121 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/30/05.

Claim Rejections - 35 USC § 112, Second Paragraph

- [7]** The rejection of claims 44 and 115-120 under 35 U.S.C. 112, second paragraph, as being unclear as to what in claim 38 has the atomic coordinates of Table 2 is

Art Unit: 1656

maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. The Courts generally accept as fact an examiner's finding that is undisputed by applicant. See *In re Kunzmann*, 140 USPQ 235 (CCPA 1964).

Claim Rejections - 35 USC § 112, First Paragraph

[8] The new matter rejection of claims 38-45 and 114-120 are rejected under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in the prior Office action.

RESPONSE TO ARGUMENT: Addressing the new matter of claim 38, applicant notes the examiner appears to acknowledge the specification contains support for language of the amendment, but states the specification "fails to support a model of *any* liganded/unliganded GR polypeptide structure having any structural coordinates." Applicant requests further clarification of the rejection, because, according to applicant, the disclosure at pp. 31 and 33 of the specification provide descriptive support for the claimed invention.

Applicant's argument is not found persuasive. As noted in the prior Office action, "[t]he cited disclosure at p. 31, ll. 9-15 of the specification describes a GR/FP/TIF2 structure having the structural coordinates of Table 2, which fails to support a model of *any* liganded/unliganded GR polypeptide structure having any structural coordinates" (prior Office action at p. 6, top). In order to comply with applicant's request, it is noted that the species of GR/FP/TIF2 structure having the structural coordinates of Table 2

with an expanded binding pocket volume of Chains A and B as recited in claim 38 fails to provide descriptive support for the recited genus of *any* liganded/unliganded GR polypeptide structure having any structural coordinates as encompassed by the claims.

Addressing the new matter limitation of claim 115, it is noted that the examiner inadvertently directed the rejection to claim 115, where the rejection was intended to be directed to claim 114. That the intent was to address the limitation of claim 114 instead of claim 115 is clear as the Office action states the limitation at issue is where "the GR polypeptide [is limited] to being 'comprised within a polypeptide complex which further comprises a co-activator,'" particularly as this is the only claim that recites this limitation. In this case, while the specification would appear to support practicing the method using a structure of a complex of GR/FP/co-activator, the examiner can find no support for practicing the method of claim 38 using only a binary complex between GR and a co-activator.

Applicant is invited to show support for the limitations at issue in the claims.

[9] The written description rejection of claims 38-43, 45, 114, and 120 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in the prior Office action. New claim 122 is included in the rejection. Thus, claims 38-43, 45, 114, 120, and 122 are rejected.

RESPONSE TO ARGUMENT: Applicant argues the description of the genus of structures encompassed by claim 38 is not based on a single disclosed representative species. Rather, applicant argues the specification provides distinguishing structural

Art Unit: 1656

characteristics of the genus of recited structures. According to applicant, two working examples of the claimed method are disclosed, and that the specification discloses sufficient detailed, relevant, identifying characteristics to describe the GR polypeptide structures encompassed by the claims.

Applicants' argument is not found persuasive. The examiner maintains the position that the specification fails to describe the genus of recited atomic coordinates of a GR polypeptide structure and the corresponding 3-D structures thereof and the genus of GR polypeptides used in the assay for GR-mediated activity. According to MPEP § 2163, when there is substantial variation within the genus, the specification should disclose a representative number of species of a recited genus to reflect the variation among the members of the genus. Applicant does not dispute the widely variant species that are encompassed by the genus. It is acknowledged that the claims require an expanded binding pocket in the "A-subunit" and the "B-subunit" of a particular volume relative to a "corresponding subunit of the GR/dexamethosone structure" as recited in the claims. However, other than limiting the volume of the pocket volumes of the A- and B-subunits, the recited structural characteristics of the GR polypeptide is unlimited. As noted in the prior Office action, the specification discloses only a *single* representative species of the genus of recited atomic coordinates and structures thereof having an expanded or large pocket volume, *i.e.*, the GR/FP/TIF2 structure having structural coordinates of Table 2. That the specification discloses only a single species of the genus of GR structures having an expanded or large pocket volume is undisputed by applicant. According to MPEP 2163, "[f]or inventions in an unpredictable art, adequate

written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." As such, the single disclosed species of structural coordinates and corresponding 3-D structures fails to reflect the variation within the genus.

Also, the specification discloses only two representative species of the genus of recited GR polypeptides, *i.e.*, SEQ ID NO:6 and 8. In this case, the genus of atomic coordinates and corresponding 3-D structures or GR polypeptides encompasses species that are *widely* variant and the single disclosed species of genus of recited atomic coordinates and structures thereof having an expanded or large pocket volume and the two disclosed species of GR polypeptides fail to reflect the variation of the members of the genus. Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[10] The scope of enablement rejection of claims 38-43, 45, 114, and 120 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in the prior Office action. New claim 122 is included in the rejection. Thus, claims 38-43, 45, 114, 120, and 122 are rejected.

RESPONSE TO ARGUMENT: Addressing claims 38-43, 114, and 120, applicant argues the presence of one working example should not be the basis of the rejection, rather one must evaluate all relevant facts and evidence. Applicant argues the only

evidence offered by the examiner in support of the undue experimentation position is applicant's specification at pp. 7-8, which describes the use of structural prediction in the absence of crystallographic data. Applicant argues the structure of a GR polypeptide complex with an expanded pocket volume has been resolved and the section of the specification as noted above is not relevant to the enablement issue. Addressing claim 45, applicant argues methods for assaying GR activity are well-known in the prior art and the specification need only disclose one method making and using the claimed invention to satisfy the enablement requirement.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification fails to enable the full scope of the claimed invention without undue experimentation. Addressing applicant's argument regarding claims 38-43, 114, and 120, it is noted that the instant rejection does not rely solely on the disclosure of a single working example. Rather, the rejection presents an analysis of the relevant Factors of *In re Wands*, which includes the presence or absence of one working example within the scope of the claims. In this case, the claims are overly broad, encompassing the use of any structure of GR having any structural coordinates that has the increased volume as recited in the claims, which is undisputed by applicant. In this case, the specification discloses only a single working example of structural coordinates that can be used to generate a structure that has such an expanded binding pocket, *i.e.*, the structural coordinates of Table 2. Further, the specification discloses only a single working example of a GR structure having an expanded binding pocket that is useful for identifying binding compounds, *i.e.*, the structure of a GR/FP/TIF2

complex having the structural coordinates of Table 2. While methods for generating homology models of a given structure were known at the time of the invention, the specification fails to disclose any relevant guidance for determining whether any other structures of a "GR polypeptide structure" as encompassed by the claims represent a *biologically relevant* form of a GR polypeptide. It is just as likely that other 3-D structures of GR polypeptides as encompassed by the claims represent inactive GR polypeptides. Applicant's own specification acknowledges the high level of unpredictability in using homology models for identifying ligands intended for a biological use. See specification at p. 7, line 23 to p. 8, line 19. While applicant attempts to dismiss these admissions of unpredictability, it is noted that neither the specification nor the prior art teaches or provides guidance for generating the atomic coordinates of GR complexes with an expanded binding volume as encompassed by the claims – other than the GR complex having the structural coordinates of Table 2 – and thus, presumably, one of skill in the art would utilize homology modeling to generate other coordinate data, which as noted by the specification, is highly unpredictable. That using homology models for ligand screening is highly unpredictable is further evidenced by the reference of Flower ("Drug Design, Cutting Edge Approaches," Royal Society of Chemistry, Cambridge, UK, 2002), which, addressing the use of homology models as representing a functional and biologically relevant conformation of a polypeptide, discloses "[p]roblems still exist, however: the fitting together of protein domains in a multi-domain protein, the determination of the most likely conformation of protein loops, the correct positioning of amino acid side chains, flexible ligand docking - to name only a few" (p. 25, middle). In

Art Unit: 1656

view of the broad scope of the claims, the lack of guidance and working examples, and the high level of unpredictability in using other structures of GR with no expectation that such structures represent a biologically relevant form of a GR polypeptide, a significant amount of non-routine experimentation is required to confirm whether any alternative structure of a GR polypeptide as encompassed by the claims is useful in accordance with the asserted utility of the claimed methods.

In response to applicant's argument regarding claim 45, it is noted that the rejection is not directed to the scope of GR assay methods *per se*, rather the rejection is directed to the scope of GR polypeptides used in the assay. As noted in the prior Office action, the claim is so broad as to encompass any method for screening using any GR polypeptide. However, the specification discloses two working examples of GR polypeptides, *i.e.*, SEQ ID NO:6 and 8. Other than these two working examples, the specification fails to provide any guidance for altering the structures of SEQ ID NO:6 and 8 with an expectation of obtaining a GR polypeptide that has the desired activity/utility. While methods of generating variants of a given polypeptide and methods of isolating homologous polynucleotides, *e.g.*, hybridization, were known, it was not routine in the art to screen for or make *all* GR polypeptides from any source having a substantial number of substitutions or modifications as encompassed by the instant claims. This is undisputed by applicant.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation is

Art Unit: 1656

necessary for a skilled artisan to make and use the entire scope of the claimed invention. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

[11] The rejection of claims 38-45 and 114-120 under 35 U.S.C. 103(a) as being unpatentable over Apolito et al. (WO 03/015692; cited in the IDS filed 5/3/2004) in view of *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir. 2004) is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. Newly added claim 122 is included in the instant rejection for the same reasoning that applies to claim 38. Thus, claims 38-45, 114-120, and 122 are rejected.

[12] The rejection of claims 38-44 and 114-120 under 35 U.S.C. 103(a) as being unpatentable over Gillner et al. (WO 00/52050; cited in the IDS filed 5/3/2004) in view of *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir.

Art Unit: 1656

2004) is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. Newly added claim 122 is included in the instant rejection for the same reasoning that applies to claim 38. Thus, claims 38-44, 114-120, and 122 are rejected.

[13] The rejection of claim 45 under 35 U.S.C. 103(a) as being unpatentable over Gillner et al. (WO 00/52050; cited in the IDS filed 5/3/2004) in view of *In re Gulack* 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir. 2004) as applied to claims 38-44, 114-120, and 122 above and further in view of Högger et al. (*Steroids* 59:597-602; cited in the prior Office action) is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

[14] RESPONSE TO ARGUMENT: According to applicant, no reasoning is provided to support the assertion that the structural coordinate data as recited in the claims is non-functional descriptive material and should not be accorded patentable weight. Applicant argues that because the recited structural coordinate data is used in the claimed methods, it represents a functional element of the methods and should be accorded patentable weight. Applicant argues the *Gulack* and *Ngai* cases are non-analogous as these cases were directed to the issue of printed matter. According to applicant, the instant claims rely on a novel structure rather than printed matter to distinguish the claimed invention over the prior art.

Applicant's argument is not found persuasive. Contrary to applicant's assertion that no reasoning has been presented to support the examiner's position that the recited structural data is non-functional descriptive material, it is noted that the examiner has clearly indicated that the recited structural coordinates are non-functional descriptive material (see, e.g., p. 13, bottom, of the prior Office action) and has pointed out relevant portions of MPEP where the subject of non-functional descriptive material is discussed and defined, thus providing ample reasoning as to how and why the recited structural coordinates are considered to be non-functional descriptive material. As noted in the prior Office action, non-functional descriptive material is "descriptive material [that] is not functionally related to the substrate" and "will not distinguish the invention from the prior art in terms of patentability."

In this case, the recited structural coordinate data appear to be used merely as input for a known computer algorithm that, in combination with the elements of the computer, generates a three-dimensional protein structure. In other words, the data do not affect how the computer performs or functions – the computer would appear to function in the same way regardless of whether or not the data is stored in a computer's machine-readable data storage medium. The examiner's position that the recited coordinate data is non-functional descriptive material is further supported by MPEP 2106.VI, which provides "[c]ommon situations" that involve nonfunctional descriptive material, including "a computer-readable storage medium that differs from the prior art solely with respect to nonfunctional descriptive material, such as music or a literary work, encoded on the medium" and "a computer that differs from the prior art solely with

Art Unit: 1656

respect to nonfunctional descriptive material that cannot alter how the machine functions (i.e., the descriptive material does not reconfigure the computer).” These “common situations” are analogous to the instantly claimed method that differs from the prior art method solely with respect to the non-functional descriptive material of the coordinate data, which does not alter how the computer functions. According to MPEP 2106.01, “‘functional descriptive material’ consists of data structures and computer programs which impart functionality when employed as a computer component. (The definition of ‘data structure’ is ‘a physical or logical relationship among data elements, designed to support specific data manipulation functions’” (emphasis added) and that “‘Nonfunctional descriptive material’ includes but is not limited to music, literary works, and a compilation or mere arrangement of data””. In this case, the method involves using a computer and a known algorithm to transform the data into a 3-D macromolecular structure. The structural coordinates appear to be an arrangement of data and do not appear to affect how the computer performs or functions and the computer would appear to function in the same way regardless of whether or not the data is stored in a computer’s machine-readable data storage medium, in the same way as music or a literary work stored on a computer would not affect its function. Contrast the atomic coordinate data with the data structure of *Lowry*, which, according to MPEP 2106.01, when stored on a computer readable medium, increases computer efficiency. As noted above, there is no evidence of record that the recited structural data interact with other computer hardware or software to affect the efficiency or accuracy or any other characteristic of computer processing. Consequently, for the reasons of record

Art Unit: 1656

and those stated above, the claimed invention would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

[15] Status of the claims:

Claims 38-45 and 113-122 are pending.

Claims 113 and 121 are withdrawn from consideration.

Claims 38-45, 114-120, and 122 are rejected.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656